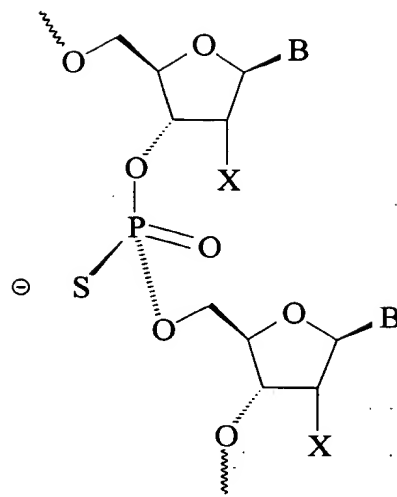


Rp isomer



Sp isomer

Figure 1

ISIS-4288 SHEET 1

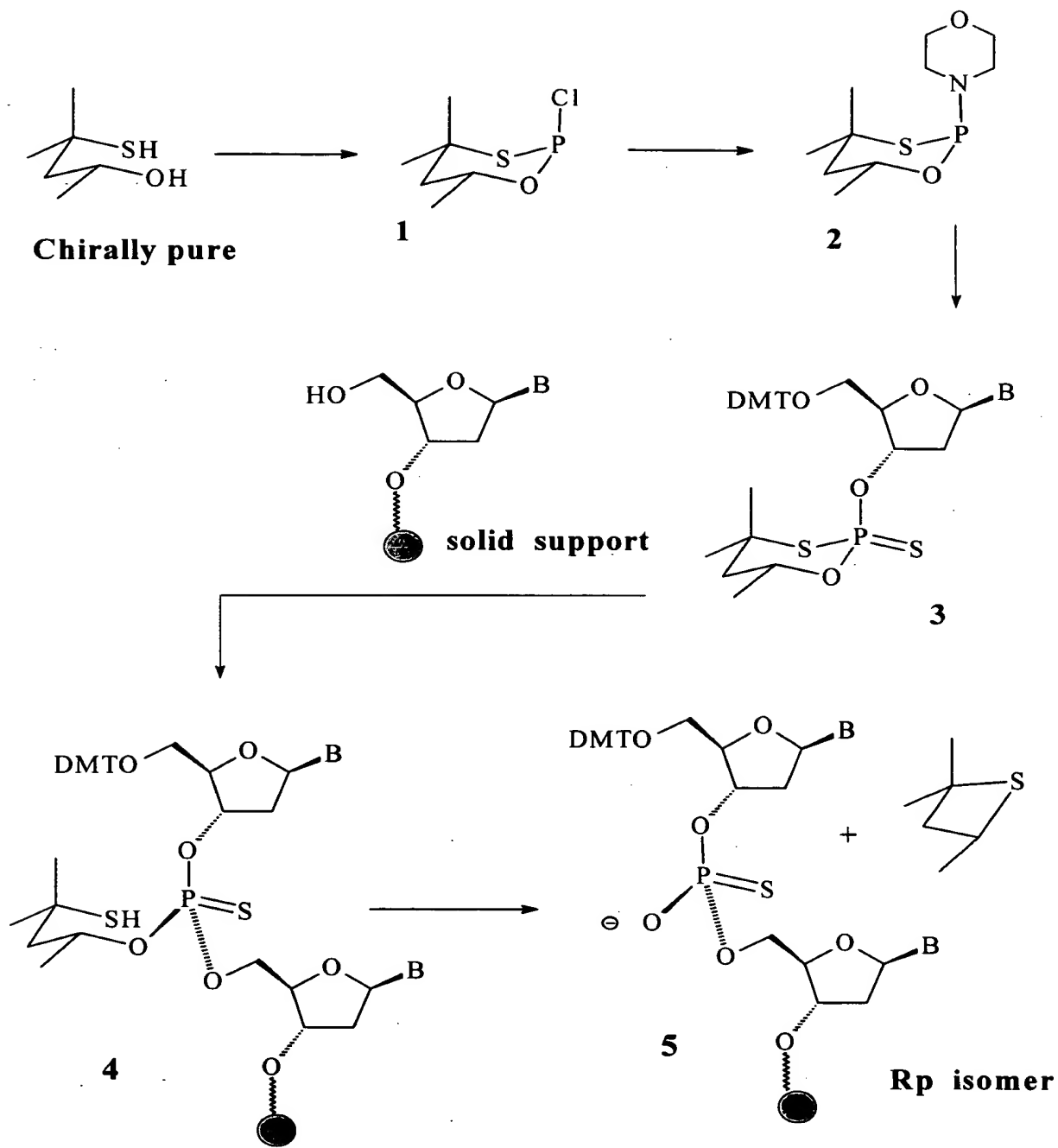


Figure 2



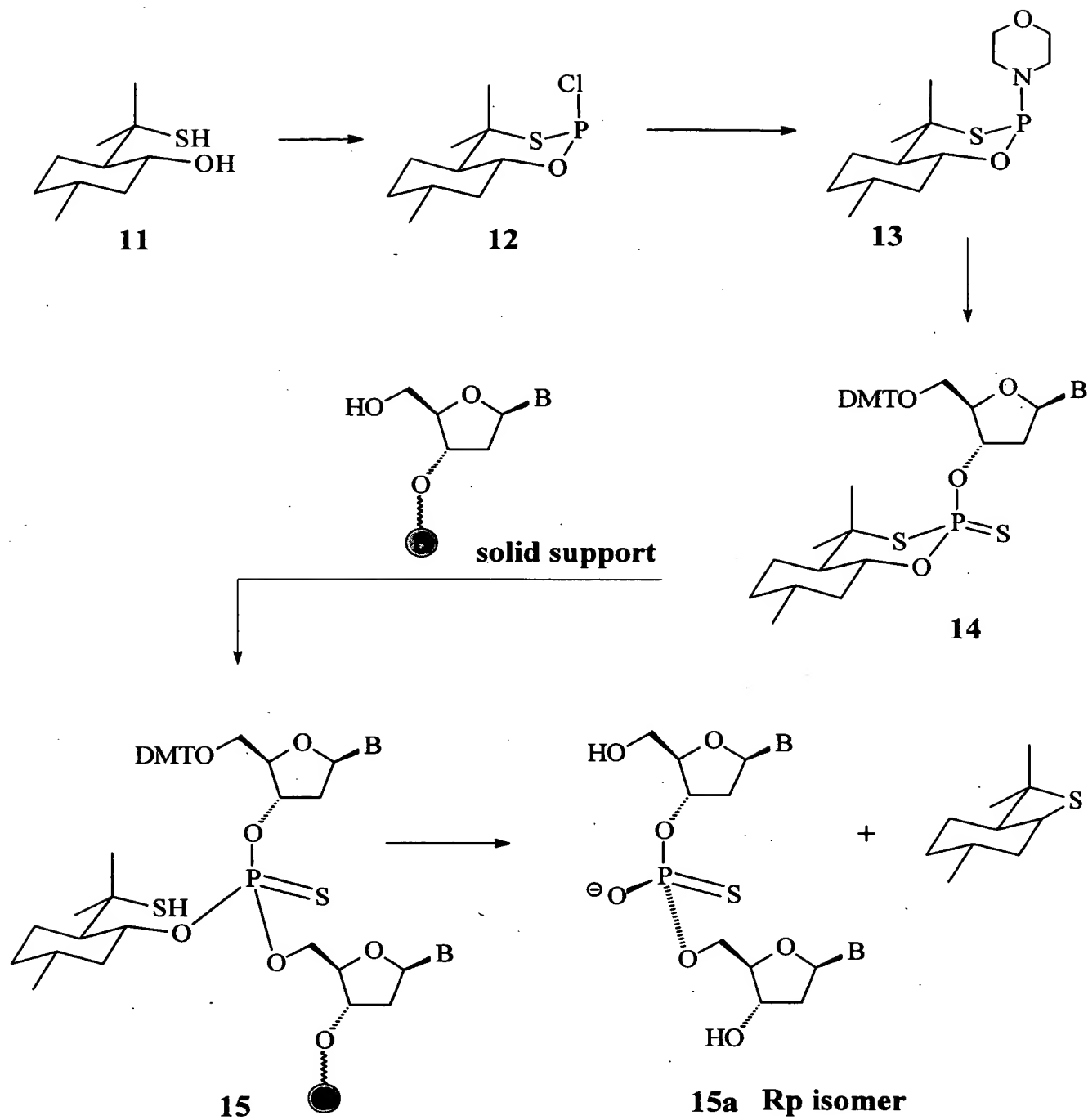


Figure 4



Figure 5

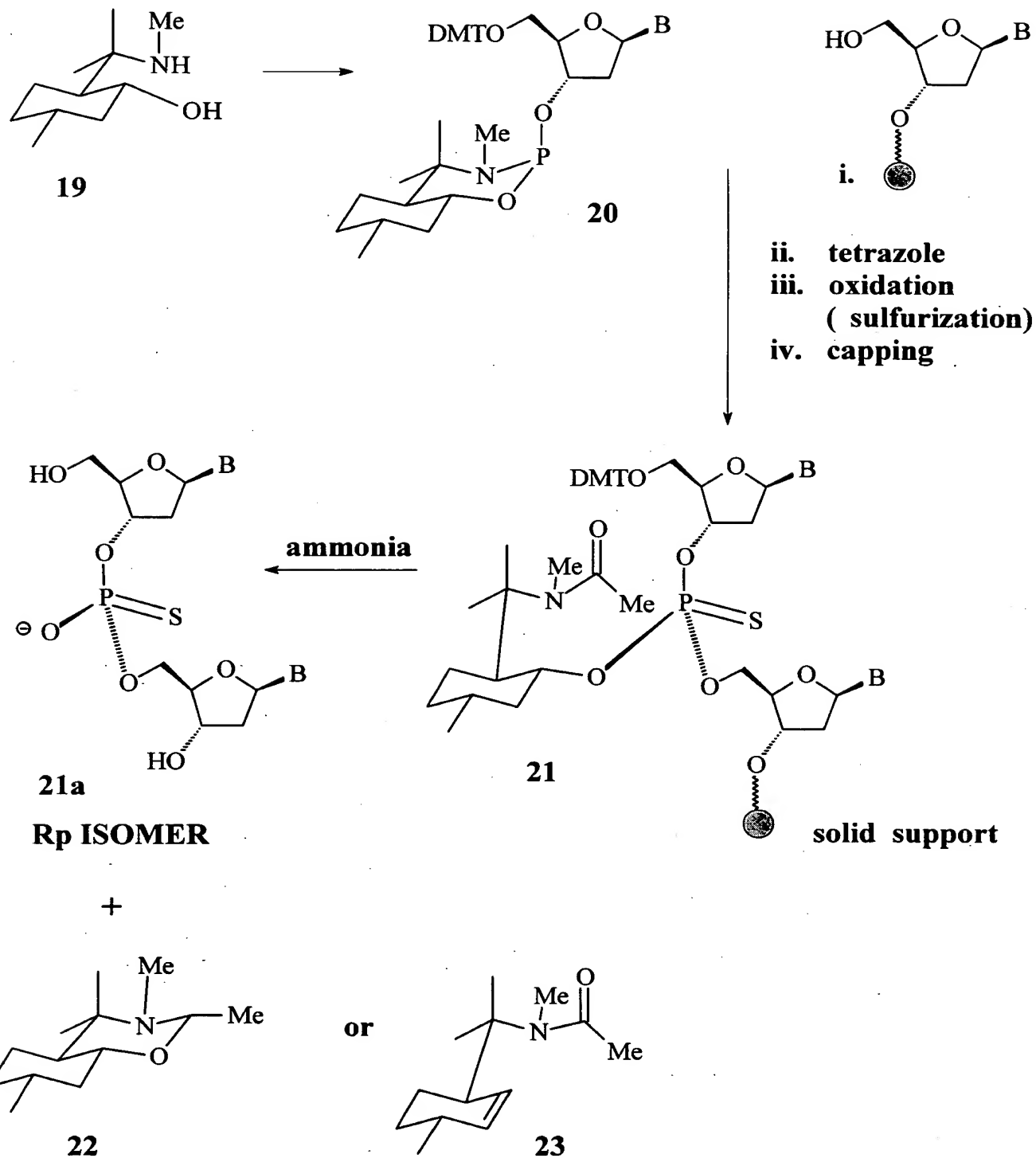


Figure 6

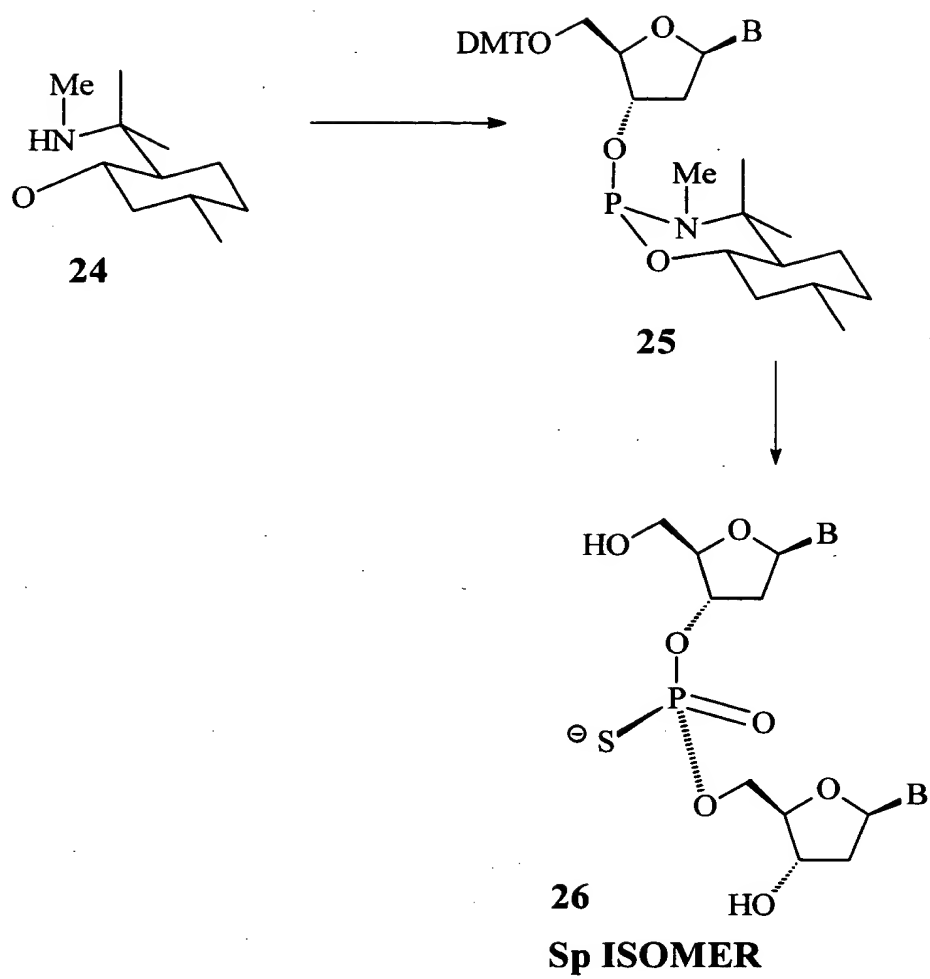
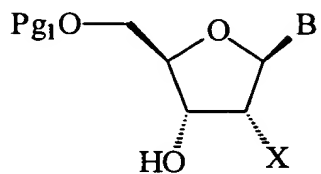


Figure 7

Building-Blocks: 5'-Pieces



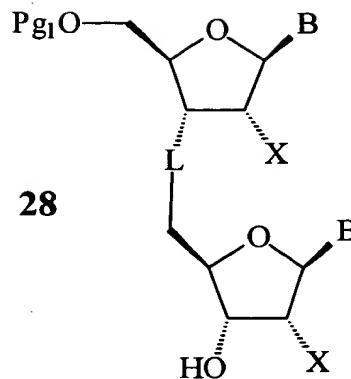
27

B = Base/Heterocycle

X = 2'-substituent group

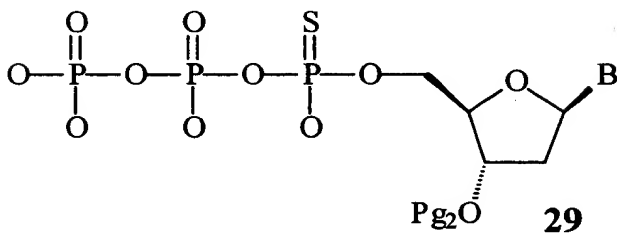
L = Linker, PS, dimer, trimer

Pg₁ = Protecting group

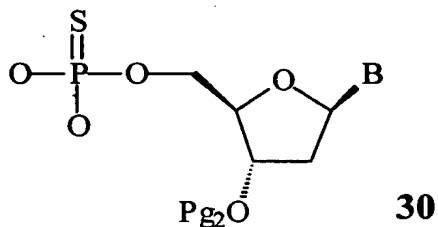


28

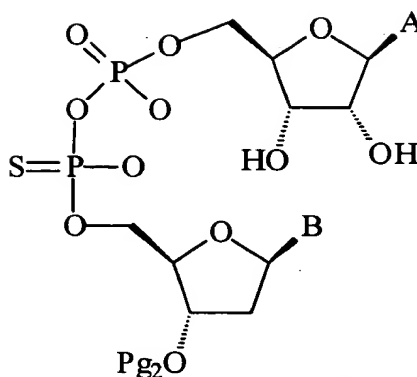
Building-Blocks: Pieces



29



30



31

Figure 8

Building-Blocks: 3'-Pieces

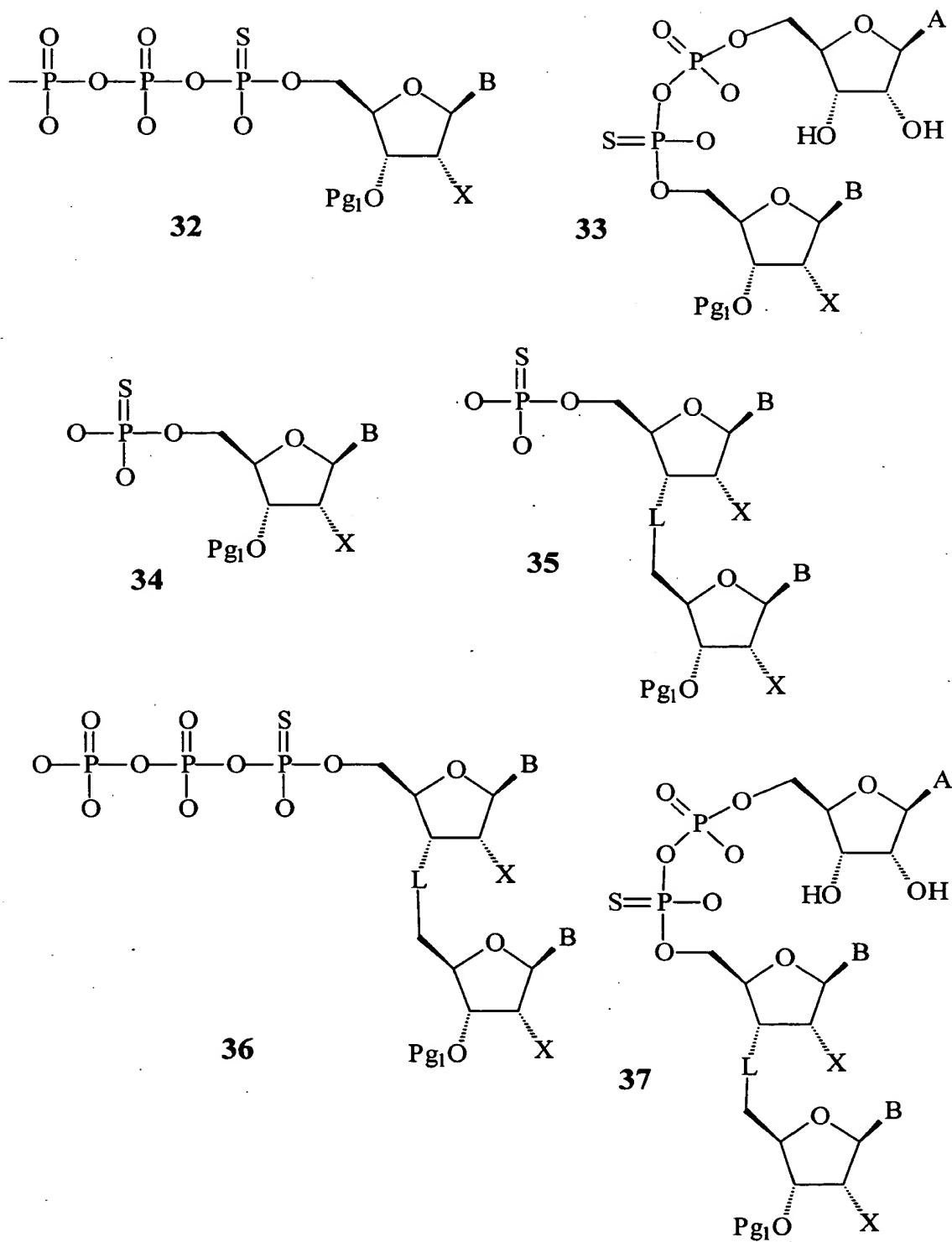
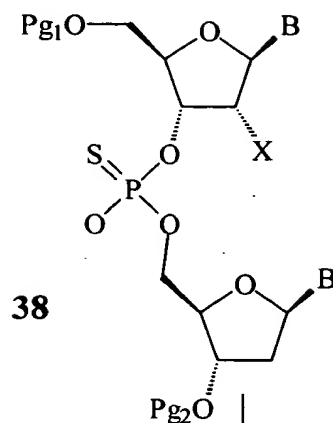


Figure 9

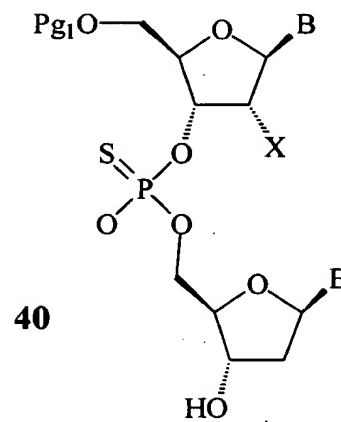
Step 1: Coupling of 5'-Piece with Middle Block

27 + 29/30/31



Step 2: Removal of Pg₂

39



Step 3: Repeat Coupling

41

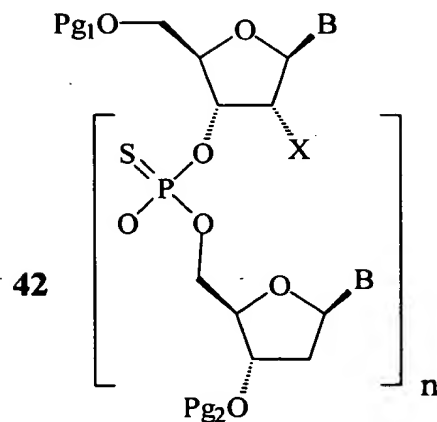
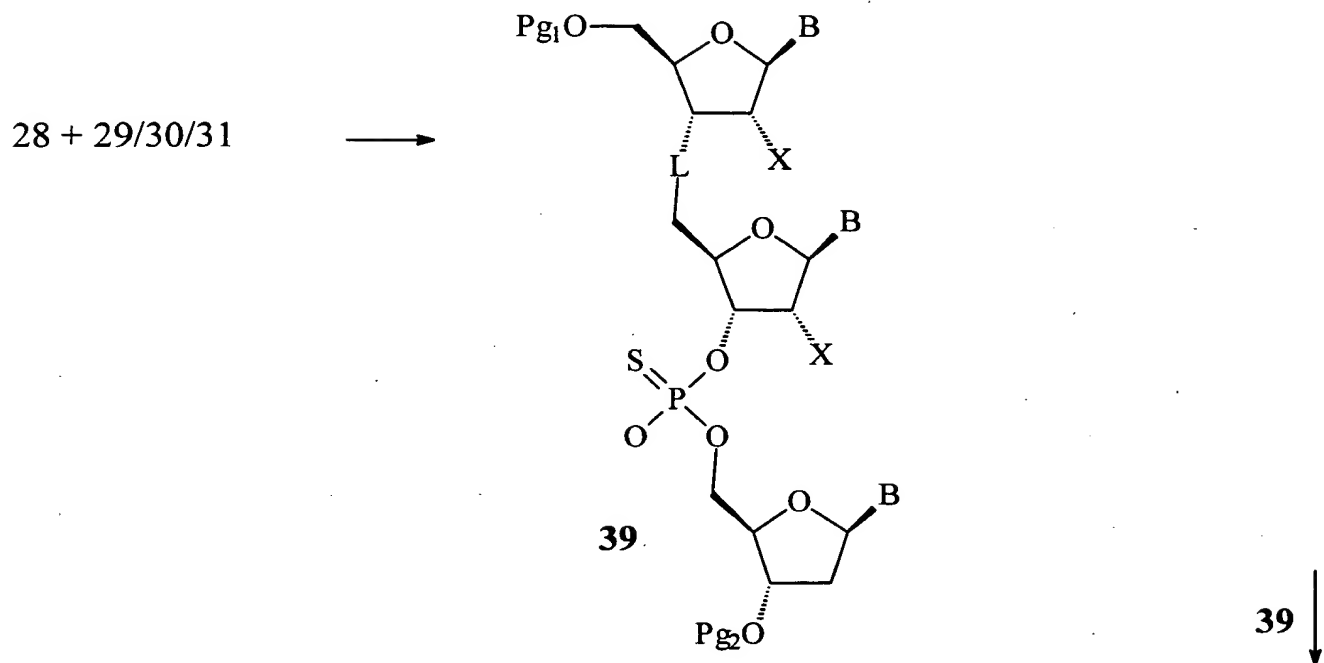
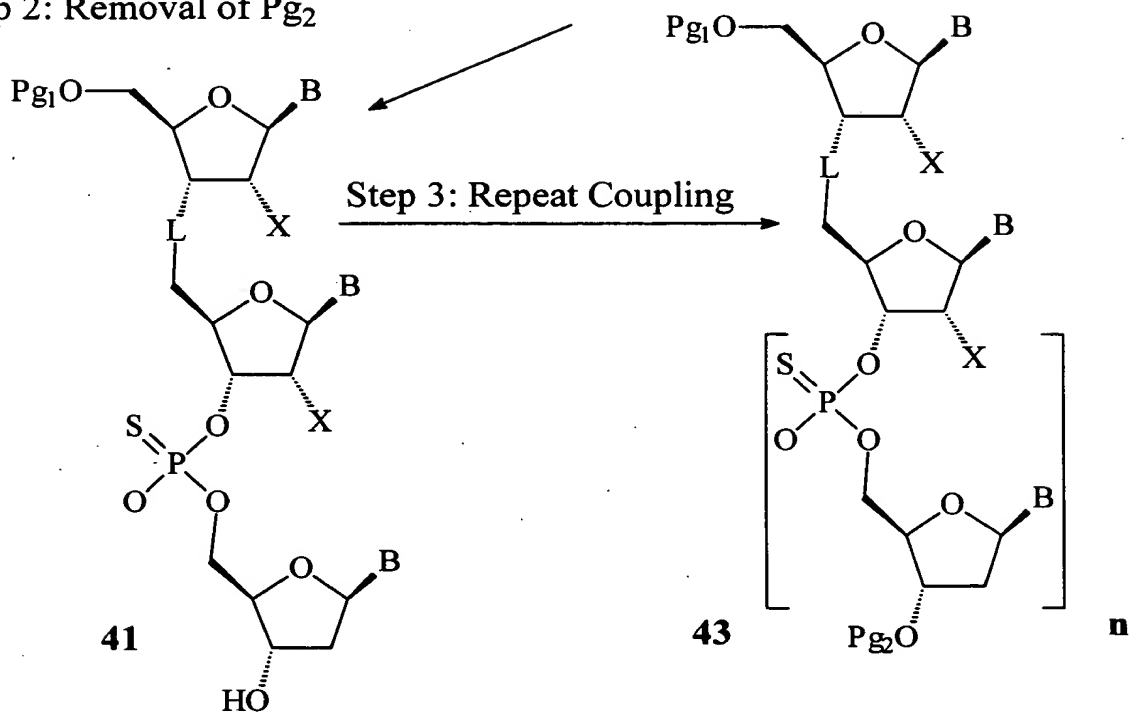


Figure 10

Step 1: Coupling of 5'-Piece with Middle Block



Step 2: Removal of Pg₂



39 ↓

41 ↓

Figure 11

Step 4: Repeat Removal of Pg_2

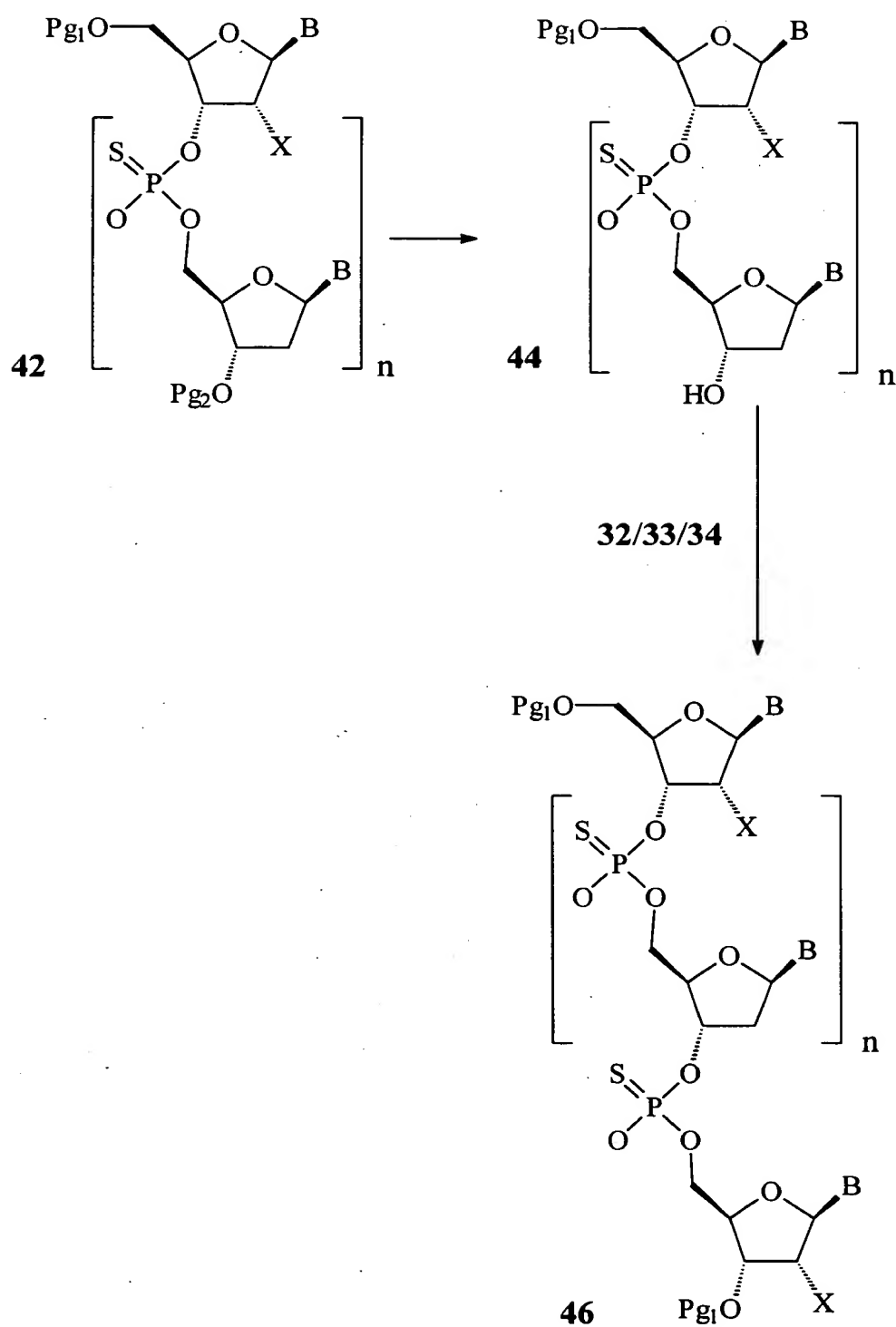


Figure 12

Step 5: Coupling with 3'-Pieces

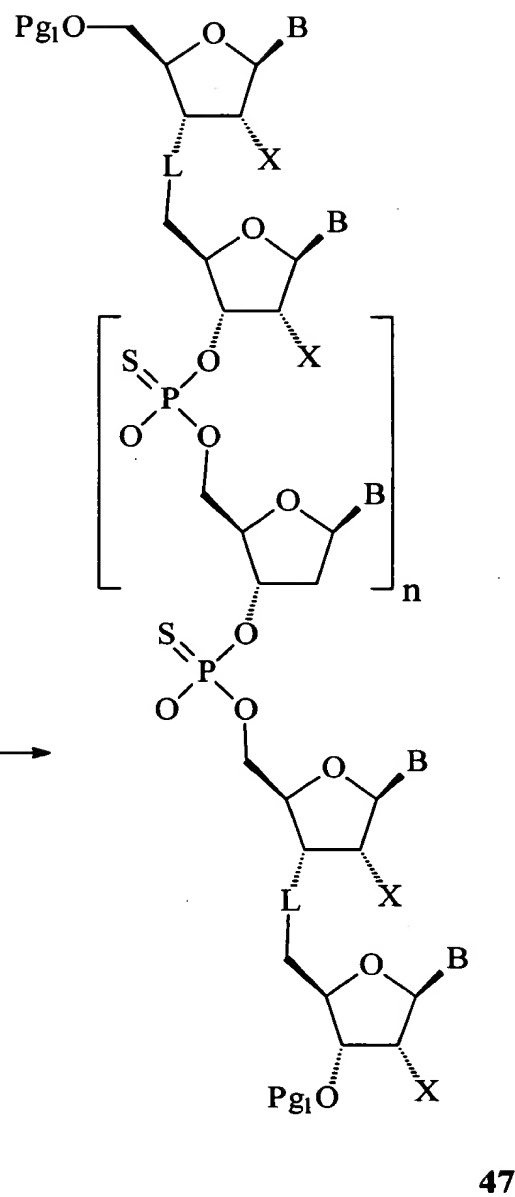
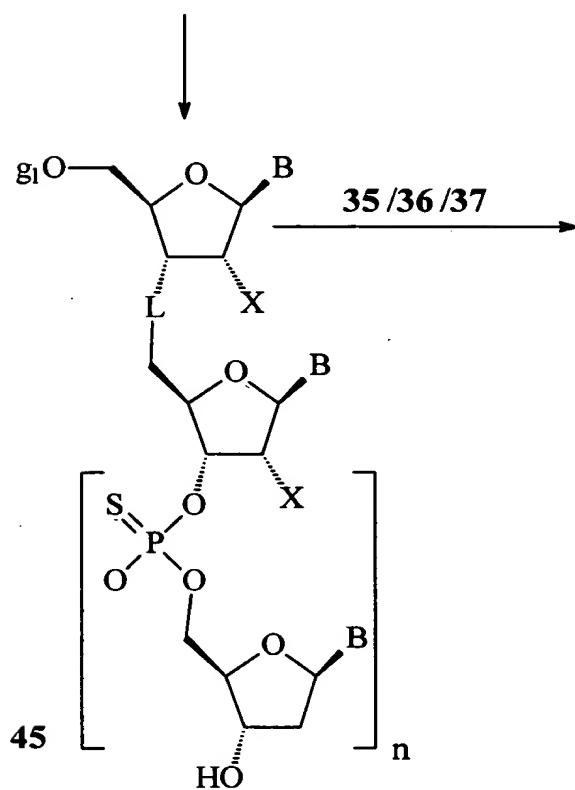
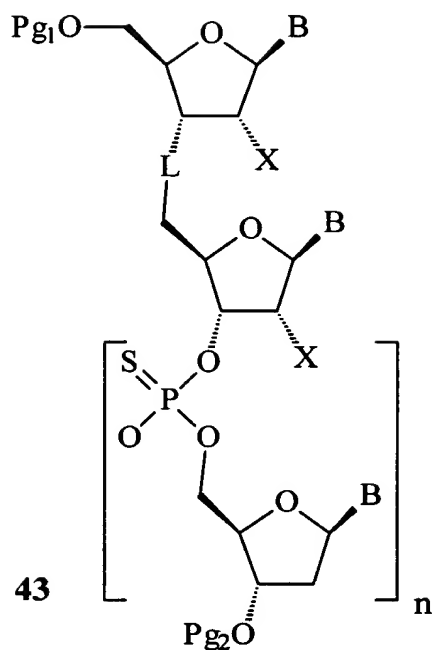


Figure 13

Step 6: Removal of Pgl

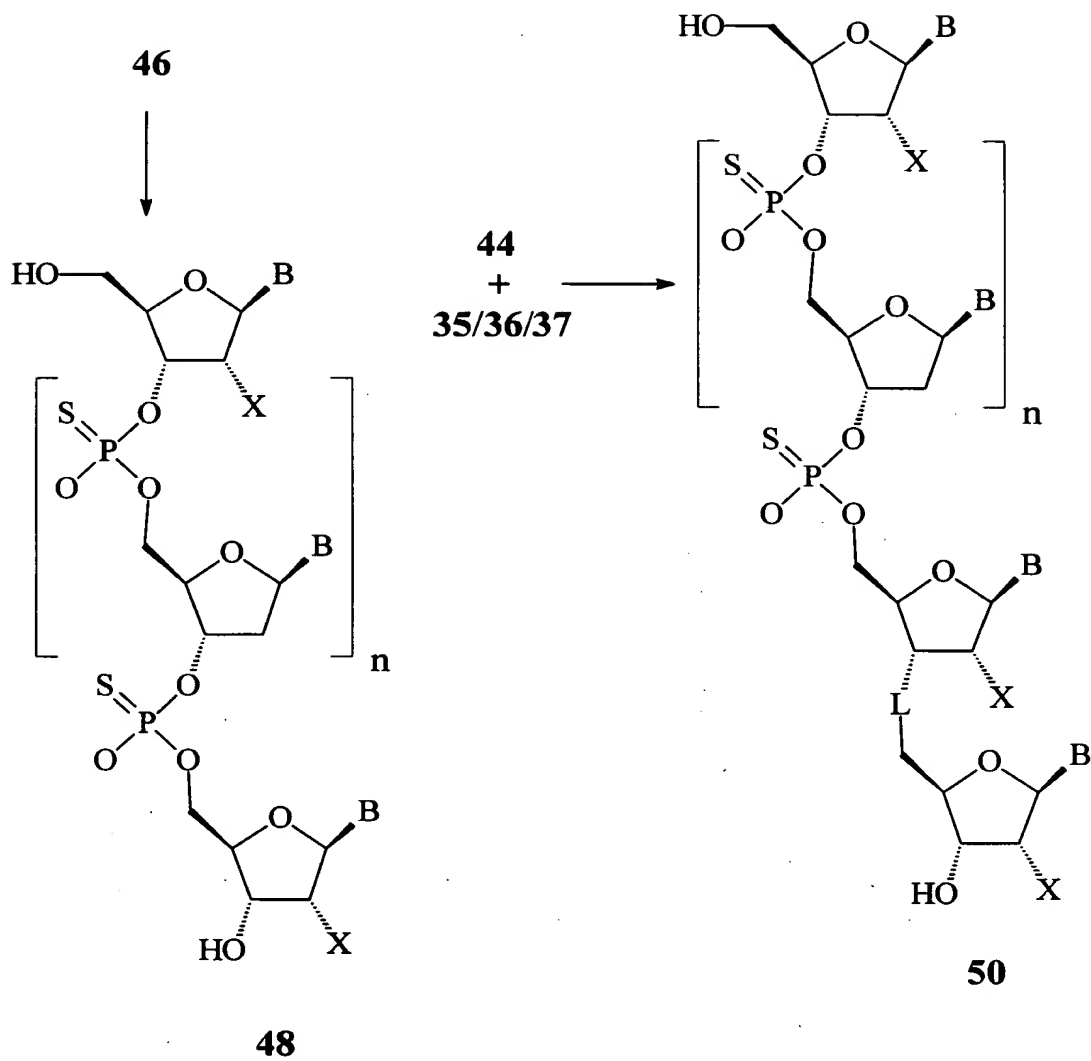


Figure 14

Step 6: Removal of Pgl

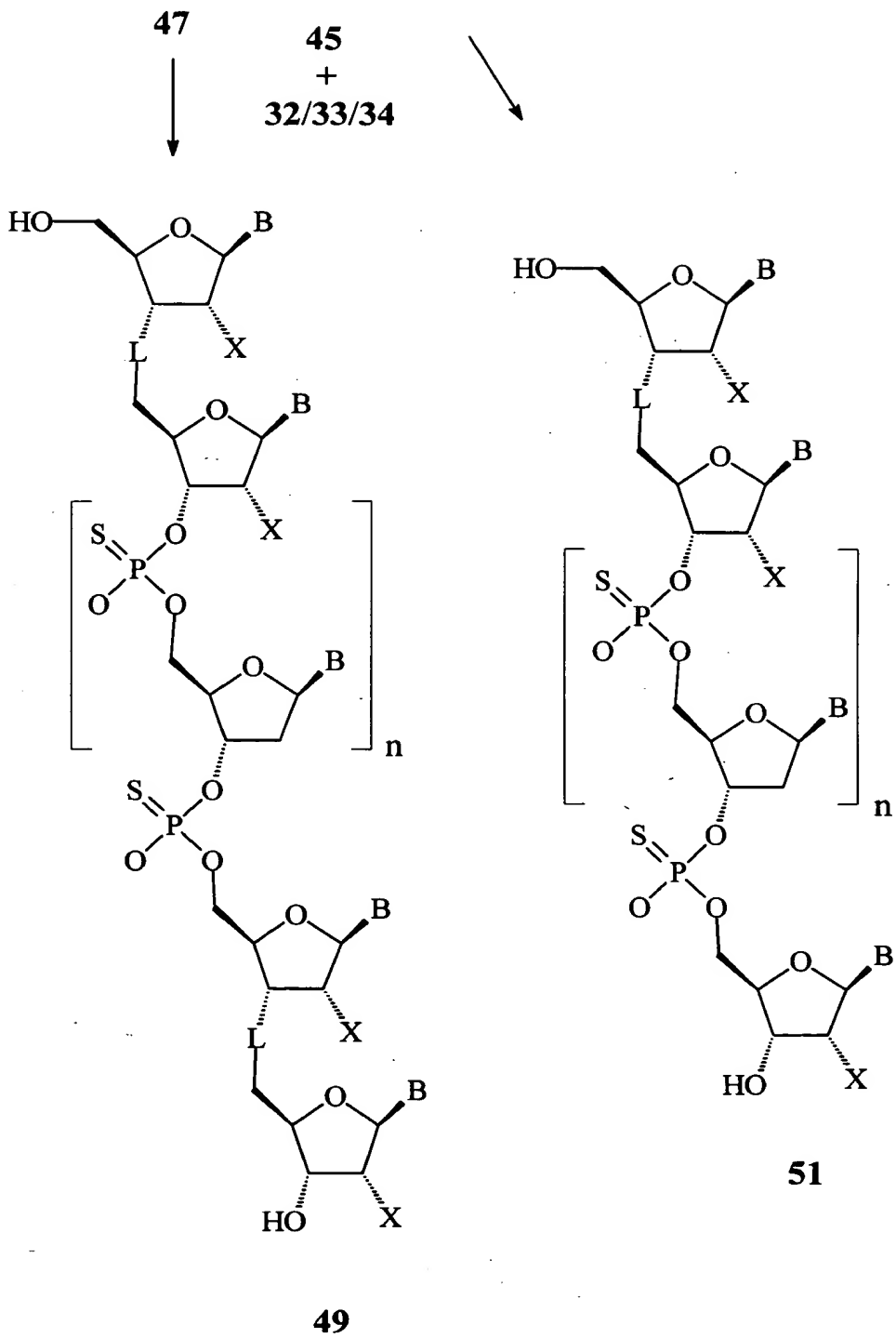


Figure 15